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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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EXAMINER	
ZHENG, LI	

ART UNIT	PAPER NUMBER
1638	

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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/561,720	ALLISON, RICHARD F.	
	Examiner	Art Unit	
	LI ZHENG	1638	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *08 February 2008*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *236-306* is/are pending in the application.

4a) Of the above claim(s) *242,259 and 275-306* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *236-241, 243-258 and 260-274* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *22 December 2005* is/are: a)☐ accepted or b)☒ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *12/22/2005*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

1. Claims 236-306 are pending.

Election/Restrictions

2. Applicant's election of Group I, claims 236-274, including an enzyme as Species I and turnip mosaic potyvirus IRES as Species II in the reply filed on 2/8/2008 is acknowledged.

Applicants do not specify the election was made with or without traverse. Since Applicants do not present any argument in the response, the election is regarded as an election made without traverse.

Claims 242, 259 and 275-306 are withdrawn for being drawn to non-elected inventions or species.

Claims 236-241, 243-258 and 260-274, including an enzyme as Species I and turnip mosaic potyvirus IRES as Species II, are examined on the merits.

The requirement is deemed proper and is therefore made FINAL.

Specification

3. The disclosure is objected to because it contains an embedded hyperlink and/or other form of browser-executable code. Applicant is required to delete the embedded

hyperlink and/or other form of browser-executable code. See MPEP § 608.01. See, for example, pages 19 and 22.

4. The specification is objected to under 37 CFR 1.821(d) as failing to refer to a sequence by use of its sequence identifier preceded by "SEQ ID NO:". The nucleotide sequences in Figure 6 should be identified by SEQ ID NOs:. Alternatively, the brief descriptions of those figures on paragraph [0043] can be amended to recite the identifiers.

5. The specification is objected to because paragraphs [0065](partial)-[0075] (partial) are missing.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Scope of Enablement

6. Claims 236-241, 243-258 and 260-274 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a method of producing a

heterologous polypeptide in plant comprising a) providing a transgenic plant comprising a DNA molecule containing a promoter operably linked to a DNA sequence containing a sequence complementary to a coding sequence for a heterologous polypeptide, a sequence complementary to an IRES from a plant virus and a 3' UTR of a first positive strand single-stranded RNA virus; b) growing the transgenic plant ; and c) stimulating synthesis of an RNA complementary to an RNA transcript of the recombinant DNA by infecting the transgenic plant with a second positive strand single-stranded RNA virus closely related to the first one, does not reasonably provide enablement for a method for producing heterologous polypeptide in any cell or any IRES from any source or any stimulus for synthesis of an RNA complementary to an RNA transcript of the recombinant DNA. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make/use the invention commensurate in scope with these claims.

The claimed invention is not supported by an enabling disclosure taking into account the *Wands* factors. *In re Wands,* 858/F.2d 731, 8 USPQ2d 1400 (Fed. Cir. 1988). *In re Wands* lists a number of factors for determining whether or not undue experimentation would be required by one skilled in the art to make and/or use the invention. These factors are: the quantity of experimentation necessary, the amount of direction or guidance presented, the presence or absence of working examples of the invention, the nature of the invention, the state of the prior art, the relative skill of those in the art, the predictability or unpredictability of the art, and the breadth of the claim.

The instant claims are drawn to a method of producing a heterologous polypeptide in any transgenic cell comprising a) providing a transgenic cell comprising a DNA molecule containing a promoter operably linked to a DNA sequence containing a sequence complementary to a coding sequence for a heterologous polypeptide, a sequence complementary to any IRES and a 3' UTR of a first positive strand single-stranded RNA virus; b) growing the transgenic cells; and c) provide stimulus for synthesis of an RNA complementary to an RNA transcript of the recombinant DNA, the DNA molecule used in the method and the transgenic cells produced by the method.

The specification prophetically teaches a method for producing a heterologous polypeptide in any transgenic cell (paragraphs [0082]-[0084]). The specification describes various promoters (paragraph [0047]), the heterologous genes (paragraph [0048]), the IRES elements (paragraphs [0049]-[0053]), 3'UTR regions (paragraphs [0054]-[0060]) and viruses that can be used as stimulus (paragraphs [0061]-[0063]). The specification also teaches that the replication complex of BMV could recognize and synthesize a complementary copy of a CCMV transgene that contains a complete 3' UTR (paragraph [0080])

The specification fails to reduce the invention to practice. The only working example is only to demonstrate that the replication complex of BMV could recognize and synthesize a complementary copy of a CCMV transgene that contains a complete 3' UTR. The working example does not use IRES to drive the translation of the heterologous gene. The claims, however, are broadly drawn to a method for producing

heterologous polypeptides in any cell using any IRES from any source or any stimulus for synthesis of an RNA complementary to an RNA transcript of the recombinant DNA.

Gleba et al. (2004, US Patent Application Publication Number 2004/0055037) teach that IRES elements isolated from animal viruses do not support translation in plant cells (paragraph [0013]).

Teycheney et al. (2000, Journal of General Virology 81:1121-1126) teach that when transgenic plants expressing LMV constructs were infected by various potyviruses, PepMoV could stimulate replication whereas a closely related virus, PVY, could not (the paragraph bridging pages 1124-1125). Teycheney et al. further teach that the state of art does not permit pinpointing specific motifs or secondary structures involved in interactions between viral 3' UTR and their RdRps (page 1125, 3rd paragraph of left column).

Therefore, without further guidance, undue experimentation would have been required for a person skilled in the art to practice the invention in organisms other than plants, or to select any pairs of the first and second single-stranded RNA viruses, or to use any IRES elements from any sources. See *Genentech Inc. v. Novo Nordisk,* A/S (CA FC) 42 USPQ2d 1001 (Fed. Cir. 1997), which teaches that "the specification, not the knowledge of one skilled in the art" must supply the enabling aspects of the invention.

Therefore, given the claim breadth, lack of further guidance and additional working example, unpredictability of the art, undue experimentation would have been required for a person skilled in the art to practice the invention.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

7. Claims 236-241, 243-257 and 260-274 are rejected under 35 U.S.C. 103(a) as being unpatentable over Teycheney et al. (2000, Journal of General Virology 81:1121-1126) in view of Basso et al. (1994, Journal of General Virology 75:3157-3165).

The instant claims are drawn to a method of producing a heterologous polypeptide in any transgenic cell or transgenic plant comprising a) providing a transgenic cell or plant comprising a DNA molecule containing a promoter operably linked to a DNA sequence containing a sequence complementary to a coding sequence for a heterologous polypeptide, a sequence complementary to any IRES and a 3' UTR of a first positive strand single-stranded RNA virus; b) growing the transgenic cells; and c) provide stimulus for synthesis of an RNA complementary to an RNA transcript of the recombinant DNA; or wherein the promoter is CaMV 35S promoter; or wherein the heterologous polypeptide is an enzyme; or wherein the IRES is from a turnip mosaic potyvirus; or wherein the 3' UTR is from a single-stranded RNA virus having no DNA stage; or wherein the DNA sequence further comprises an intron; or wherein the

transgenic plant is N. benthamiana plant; or wherein providing stimulus for synthesis of an RNA complementary to an RNA transcript of the recombinant DNA comprising infecting the transgenic plant with a second positive strand single-stranded RNA virus with no DNA stage such as Pepper mottle virus (PepMoV) comprising sequence encoding RdRp, or the cDNA thereof. The instant claims are also drawn to the DNA construct used in the method and the transgenic plant cell/seed produced by the method

Teycheney et al teach that when expressed in transgenic tobacco plants, transgene mRNA that include 3' UTR of Lettuce mosaic virus (LMV) served as template for synthesis of complementary (-) strand RNA following an infection by PepMoV (abstract; also the paragraph bridging pages 1124-1125). LMV is well known to be a positive single-stranded RNA virus with no DNA stage. Teycheney et al teach transgene is driven by CaMV 35S promoter (Figure 1).

Teycheney et al. do not teach a sequence complementary to a coding sequence for a heterologous enzyme or a sequence complementary to an IRES from turnip mosaic potyvirus.

Basso et al. teach IRES from turnip mosaic potyvirus RNA.

Given the recognition of those of ordinary skill in the art of the value of the observation that transgene mRNA that include 3' UTR of Lettuce mosaic virus (LMV) served as template for synthesis of complementary (-) strand RNA following an infection by were infected by PepMoV as taught by Teycheney et al., it would have been obvious for a person with ordinary skill in the art to modify the transgene

construct of Teycheney et al. by replace LMVCP encoding sequence with a sequence complementary to a DNA sequence encoding the gene of interest operably linked to an IRES of Basso et al., resulting in the instant invention. One skilled in the art would have been motivated to do so given the teaching of Teycheney et al. that transgene mRNA that include 3' UTR of Lettuce mosaic virus (LMV) served as template for synthesis of complementary (-) strand RNA following an infection by were infected by PepMoV. Therefore such synthesis of complementary strand allows amplification of sense RNA encoding the gene of interest. Adding IRES of Basso et al. further allows the RNA encoding the gene of interest to be translated efficiently given the teaching of Basso et al. that the ribosomes bound to the IRES of TuMV and then scanned the sequence for the initiator AUG (abstract).

Although the combined teachings do not teach a method for producing an enzyme, such limitation is merely a design choice.

Thus the claimed invention would have been *prima facie* obvious as a whole to one of ordinary skill in the art at the time it was made, especially in the absence of evidence to the contrary.

Conclusion

No claim is allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Li Zheng whose telephone number is 571-272-8031. The examiner can normally be reached on Monday through Friday 9:00 AM - 5:30 PM EST.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Anne Marie Grunberg can be reached on 571-272-0975. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

/Anne Marie Grunberg/

Supervisory Patent Examiner, Art Unit 1638